peripheral arterial disease (PAD) in people with diabetes; (2) the biology of PAD in people with diabetes; (3) how PAD is best diagnosed in people with diabetes; and (4) appropriate treatments for PAD in people with diabetes.

Some interesting conclusions of the consensus conference are as follows:

Vascular abnormalities in people with diabetes increase with duration of diabetes and worsening blood pressure control.
People with diabetes are more prone to sudden ischemic events secondary to arterial thrombosis of underlying atherosclerotic lesions.
Abnormalities in blood rheology in people with diabetes are associated with elevations in blood viscosity and fibrinogen. Both blood viscosity and fibrinogen abnormalities have been associated with the presence, development, and complications of PAD.
Using the ankle-brachial index (ABI), the prevalence of PAD in people with diabetes >40 years of age is 20% and is as high as 29% in those >50 years of age.
All people with diabetes >50 years of age should have a screening ABI.
A screening ABI should also be considered in people with diabetes who are <50 years of age and who have other PAD risk factors such as smoking, hypertension, hyperlipidemia, or a duration of diabetes greater than 10 years.

Comment: This consensus statement comes from a panel of highly respected experts. Its recommendations are likely to have an impact on clinical care. In particular, the recommendation for screening ABIs may have immediate impact on vascular laboratories. Those who manage vascular laboratories are placed in a difficult position. The panel recommends screening ABIs, but screening studies are generally not reimbursed.

Isolation and transplantation of autologous circulating endothelial cells into denuded vessels and prosthetic grafts: Implications for cell-based vascular therapy

Griese DP, Ehsan A, Melo LG, et. al. Circulation 2003;108:2710-5.

Conclusion: Endothelial progenitor cells (EPC) may play an important role in reestablishing endothelial integrity of injured vessels. They thus may inhibit neointimal hyperplasia and improve patency of small caliber bioprosthetic grafts.

Summary: Blood-borne endothelial cells from adult bone marrow have properties of EPCs. EPCs recruited at the sites of injury may differentiate into mature endothelial cells and participate in tissue repair. A method for isolation and expression of EPCs from blood yielding sufficient numbers for potential therapeutic applications was developed. Identification of EPCs was facilitated by retrovial insertion of the bacterial LacZ gene into the EPC. In a rabbit model, balloon-injured carotid arteries and 4-mm internal diameter polytetrafluoroethylene (PTFE) grafts were evaluated for the ability of seeded EPC cells to lead to endothelialization of denuded vessels and graft segments. Endothelialization was confirmed by using staining of luminal surfaces for the endothelial cell marker CD31.

In the balloon-injured carotid arteries, 4 days after EPC seeding, >70% of the luminal surface was covered with LacZ-positive cells. No Lac-Z positive cells were visible after 4 weeks. Endothelial cell coverage at 4 days after seeding was 60% of the luminal surface in seeded arteries versus less than 5% in control vessels. EPC transplantation reduced neointimal thickening at 2 weeks ($P < .05$). At 4 weeks, in the PTFE grafts seeded with EPCs, 40% to 60% of the luminal area was covered by endothelial cells versus <5% in control grafts.

Comment: The current data may spawn a new round of research in endothelial seeding of bioprosthetic grafts, this time using bone marrow–derived EPCs as a source of endothelial cells. Such grafts could serve as arterial substitutes or as delivery mechanisms for cell-based therapy.

Arachidonate 5-lipoxygenase promoter genotype, dietary arachidonic acid, and atherosclerosis

Dwyer JH, Allayee H, Dwyer KM, et al. N Engl J Med 2004;350:29-37.

Conclusions: There is a large increase in carotid intima-media thickness among carriers of two variant 5-lipoxygenase promoter alleles compared with carriers of the common allele of 5-lipoxygenase. This effect is diminished by dietary marine n-3 fatty acids.

Summary: Atherosclerosis is a chronic inflammatory process. Leukotrienes are inflammatory mediators generated by 5-lipoxygenase from arachidonic acid. The authors speculated that polymorphism of the promoter for the 5-lipoxygenase gene could interact with dietary intake of 5-lipoxygenase substrates in a competitive fashion to promote atherosclerosis in humans. To test this hypothesis, 5-lipoxygenase genotypes, carotid intima-media thickness, markers of inflammation and measures of dietary marine n-3 fatty acids and dietary arachidonic acid were determined in 470 healthy middle-aged subjects.

Genotyping determined that 442 subjects (94%) had the common (wild type) allele of 5-lipoxygenase and 28 subjects (6%) had a variant allele. Carotid intima-media thickness adjusted for sex, height, age, and ethnicity was increased by 80 ± 19 μm (95% confidence interval, 43-116; $P < .001$) among carriers of variant alleles compared with carriers of the wild type allele. C-reactive protein, a marker of inflammation associated with atherosclerosis, was increased by a factor of 2 among subjects with the variant alleles compared with those with the wild type allele. Increased arachidonic acid in the diet enhanced the atherogenic effect of genotype, whereas increased dietary n-3 fatty acids blunted the effect.

Comment: The authors have characterized a diet/gene interaction that may lead to increased atherosclerosis. Their findings also suggest one mechanism for the apparent benefit of marine n-3 fatty acids in blunting atherosclerosis.

Plasma natriuretic peptide levels and the risk of cardiovascular events and death

Wang TJ, Larson MG, Levy D, et al. N Engl J Med 2004;350:655-63.

Conclusion: Plasma natriuretic peptide levels are predictors of death and cardiovascular events.

Summary: Natriuretic peptides are hormones involved in volume homeostasis. They are secreted from cardiomyocytes in response to ventricular or atrial wall stretch. High levels indicate heart failure. The authors prospectively examined the relationship of plasma B-type natriuretic peptide and N-terminal pro-atrial natriuretic peptide to the risk of death and major cardiovascular events (heart failure, atrial fibrillation, stroke, transient ischemic attack, and coronary heart disease) in 3346 persons without heart failure.

Mean follow-up was 5.2 years. One hundred nineteen subjects died, and 79 had a first cardiovascular event. Each increment of one standard deviation in log B-type natriuretic peptide levels was associated with a 27% increase in the risk of death ($P = .009$), a 28% increase in the risk of a first cardiovascular event ($P = .03$), a 77% increase in the risk of heart failure ($P < .001$), a 53% increase risk in stroke or transient ischemic attack ($P = .002$), and a 66% increased risk of atrial fibrillation ($P < .001$). No association was found with coronary heart disease events. B-type natriuretic peptide levels above the 80th percentile were associated with a multivariable-adjusted hazard ratio (HR) of 1.62 for death ($P = .02$), an HR of 1.76 for a first major cardiovascular event ($P = .03$), an HR of 1.99 for stroke or transient ischemic attack ($P = .02$), and an HR of 3.07 for heart failure ($P = .002$). The results were not significantly different for N-terminal pro-atrial natriuretic peptide.

Comment: The levels of natriuretic peptides found to predict cardiovascular events in this study are well below the usual thresholds for the diagnosis of heart failure. The utility of these data in clinical practice remains to be determined, but is consistent with the observation that asymptomatic markers of cardiovascular disease predict increased clinical risk.